SEQUENCE LISTING   <110> CANFIELD, WILLIAM M   <120> METHODS FOR PRODUCING HIGHLY PHOSPHORYLATED LYSOSOMAL HYDROLASES   <130> 210119US0CONT <150> 60/153,831 <151> 1999-09-14 <150> US 09/635,872 <151> 2000-08-10 <160> 52   <170> PatentIn version 3.1 <210> 1 <211> 928 <212> PRT <213> Homo sapiens <400> 1

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Arg Tyr Gly Leu Tyr Val Cys Phe Leu Gly Val Val Val Thr Ile Val
            20   25   30

Ser Ala Phe Gln Phe Gly Glu Val Val Leu Glu Trp Ser Arg Asp Gln
        35   40   45

Tyr His Val Leu Phe Asp Ser Tyr Arg Asp Asn Ile Ala Gly Lys Ser
    50   55   60

Phe Gln Asn Arg Leu Cys Leu Pro Met Pro Ile Asp Val Val Tyr Thr
65   70   75   80

Trp Val Asn Gly Thr Asp Leu Glu Leu Leu Lys Glu Leu Gln Gln Val
                85   90   95

Arg Glu Gln Met Glu Glu Glu Gln Lys Ala Met Arg Glu Ile Leu Gly
            100   105   110

Lys Asn Thr Thr Glu Pro Thr Lys Lys Ser Glu Lys Gln Leu Glu Cys
        115   120   125

Leu Leu Thr His Cys Ile Lys Val Pro Met Leu Val Leu Asp Pro Ala
    130   135   140

Leu Pro Ala Asn Ile Thr Leu Lys Asp Val Pro Ser Leu Tyr Pro Ser
145   150   155   160

Phe His Ser Ala Ser Asp Ile Phe Asn Val Ala Lys Pro Lys Asn Pro
                165   170   175

Ser Thr Asn Val Ser Val Val Val Phe Asp Ser Thr Lys Asp Val Glu
                180   185   190

Asp Ala His Ser Gly Leu Leu Lys Gly Asn Ser Arg Gln Thr Val Trp
            195   200   205

Arg Gly Tyr Leu Thr Thr Asp Lys Glu Val Pro Gly Leu Val Leu Met
    210   215   220

Gln Asp Leu Ala Phe Leu Ser Gly Phe Pro Pro Thr Phe Lys Glu Thr

Asn Gln Leu Lys Thr Lys Leu Pro Glu Asn Leu Ser Ser Lys Val Lys
                245   250   255

Leu Leu Gln Leu Tyr Ser Glu Ala Ser Val Ala Leu Leu Lys Leu Asn
                260   265   270

Asn Pro Lys Asp Phe Gln Glu Leu Asn Lys Gln Thr Lys Lys Asn Met
            275   280   285

Thr Ile Asp Gly Lys Glu Leu Thr Ile Ser Pro Ala Tyr Leu Leu Trp
    290   295   300

Asp Leu Ser Ala Ile Ser Gln Ser Lys Gln Asp Glu Asp Ile Ser Ala
305   310   315   320

Ser Arg Phe Glu Asp Asn Glu Glu Leu Arg Tyr Ser Leu Arg Ser Ile
                325   330   335

Glu Arg His Ala Pro Trp Val Arg Asn Ile Phe Ile Val Thr Asn Gly
                340   345   350

Gln Ile Pro Ser Trp Leu Asn Leu Asp Asn Pro Arg Val Thr Ile Val
                355   360   365

Thr His Gln Asp Val Phe Arg Asn Leu Ser His Leu Pro Thr Phe Ser
    370   375   380

Ser Pro Ala Ile Glu Ser His Ile His Arg Ile Glu Gly Leu Ser Gln
385   390   395   400

Lys Phe Ile Tyr Leu Asn Asp Asp Val Met Phe Gly Lys Asp Val Trp
                405   410   415

Pro Asp Asp Phe Tyr Ser His Ser Lys Gly Gln Lys Val Tyr Leu Thr
                420   425   430

Trp Pro Val Pro Asn Cys Ala Glu Gly Cys Pro Gly Ser Trp Ile Lys
            435   440   445

Asp Gly Tyr Cys Asp Lys Ala Cys Asn Asn Ser Ala Cys Asp Trp Asp
    450   455   460

Gly Gly Asp Cys Ser Gly Asn Ser Gly Gly Ser Arg Tyr Ile Ala Gly
465   470   475   480

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Gly Gly Gly Thr Gly Ser Ile Gly Val Gly His Pro Trp Gln Phe Gly
            485                 490                 495

Gly Gly Ile Asn Ser Val Ser Tyr Cys Asn Gln Gly Cys Ala Asn Ser
            500                 505                 510

Trp Leu Ala Asp Lys Phe Cys Asp Gln Ala Cys Asn Val Leu Ser Cys
        515                 520                 525

Gly Phe Asp Ala Gly Asp Cys Gly Gln Asp His Phe His Glu Leu Tyr
    530                 535                 540

Lys Val Ile Leu Leu Pro Asn Gln Thr His Tyr Ile Ile Pro Lys Gly
545                 550                 555                 560

Glu Cys Leu Pro Tyr Ser Phe Ala Glu Val Ala Lys Arg Gly Val
                565                 570                 575

Glu Gly Ala Tyr Ser Asp Asn Pro Ile Ile Arg His Ala Ser Ile Ala
            580                 585                 590

Asn Cys Trp Lys Thr Ile His Leu Ile Met His Ser Gly Met Asn Ala
        595                 600                 605

Thr Thr Ile His Phe Asn Leu Thr Phe Gln Asn Thr Asn Asp Glu Glu
    610                 615                 620

Phe Cys Met Gln Ile Thr Val Glu Val Asp Thr Arg Glu Gly Pro Lys
625                 630                 635                 640

Leu Asn Ser Thr Ala Gln Lys Gly Tyr Glu Asn Leu Val Ser Pro Ile
            645                 650                 655

Thr Leu Leu Pro Glu Ala Glu Ile Leu Phe Glu Asp Ile Pro Lys Glu
            660                 665                 670

Lys Arg Phe Pro Lys Phe Lys Arg His Asp Val Asn Ser Thr Arg Arg
        675                 680                 685

Ala Gln Glu Glu Val Lys Ile Pro Leu Val Asn Ile Ser Leu Leu Pro
    690                 695                 700

Lys Asp Ala Gln Leu Ser Leu Asn Thr Leu Asp Leu Gln Leu Glu His
705                 710                 715                 720

Gly Asp Ile Thr Leu Lys Gly Tyr Asn Leu Ser Lys Ser Ala Leu Leu
            725                 730                 735

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Arg Ser Phe Leu Met Asn Ser Gln His Ala Lys Ile Lys Asn Gln Ala
            740                 745                 750

Ile Ile Thr Asp Glu Thr Asn Asp Ser Leu Val Ala Pro Gln Glu Lys
            755                 760                 765

Gln Val His Lys Ser Ile Leu Pro Asn Ser Leu Gly Val Ser Glu Arg
    770                 775                 780

Leu Gln Arg Leu Thr Phe Pro Ala Val Ser Val Lys Val Asn Gly His
785                 790                 795                 800

Asp Gln Gly Gln Asn Pro Pro Leu Asp Leu Glu Thr Thr Ala Arg Phe
                805                 810                 815

Arg Val Glu Thr His Thr Gln Lys Thr Ile Gly Gly Asn Val Thr Lys
            820                 825                 830

Glu Lys Pro Pro Ser Leu Ile Val Pro Leu Glu Ser Gln Met Thr Lys
            835                 840                 845

Glu Lys Lys Ile Thr Gly Lys Glu Lys Glu Asn Ser Arg Met Glu Glu
    850                 855                 860

Asn Ala Glu Asn His Ile Gly Val Thr Glu Val Leu Leu Gly Arg Lys
865                 870                 875                 880

Leu Gln His Tyr Thr Asp Ser Tyr Leu Gly Phe Leu Pro Trp Glu Lys
                885                 890                 895

Lys Lys Tyr Phe Gln Asp Leu Leu Asp Glu Glu Glu Ser Leu Lys Thr
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Gln Leu Ala Tyr Phe Thr Asp Ser Lys Asn Thr Gly Arg Gln Leu Lys
            915                 920                 925

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Lys Phe Gly Phe Thr Ser Arg Lys Val Pro Ala His Met Pro His Met
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Ile Asp Arg Ile Val Met Gln Glu Leu Gln Asp Met Phe Pro Glu Glu
            35                  40                  45
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Phe Asp Lys Thr Ser Phe His Lys Val Arg His Ser Glu Asp Met Gln
    50                  55                  60

Phe Ala Phe Ser Tyr Phe Tyr Tyr Leu Met Ser Ala Val Gln Pro Leu
65                  70                  75                      80

Asn Ile Ser Gln Val Phe Asp Glu Val Asp Thr Asp Gln Ser Gly Val
                85                  90                  95

Leu Ser Asp Arg Glu Ile Arg Thr Leu Ala Thr Arg Ile His Glu Leu
                100                 105                 110

Pro Leu Ser Leu Gln Asp Leu Thr Gly Leu Glu His Met Leu Ile Asn
            115                 120                 125

Cys Ser Lys Met Leu Pro Ala Asp Ile Thr Gln Leu Asn Asn Ile Pro
    130                 135                 140

Pro Thr Gln Glu Ser Tyr Tyr Asp Pro Asn Leu Pro Pro Val Thr Lys
145                 150                 155                 160

Ser Leu Val Thr Asn Cys Lys Pro Val Thr Asp Lys Ile His Lys Ala
                165                 170                 175

Tyr Lys Asp Lys Asn Lys Tyr Arg Phe Glu Ile Met Gly Glu Glu Glu
                180                 185                 190

Ile Ala Phe Lys Met Ile Arg Thr Asn Val Ser His Val Val Gly Gln
            195                 200                 205

Leu Asp Asp Ile Arg Lys Asn Pro Arg Lys Phe Val Cys Leu Asn Asp
    210                 215                 220

Asn Ile Asp His Asn His Lys Asp Ala Gln Thr Val Lys Ala Val Leu
225                 230                 235                 240

Arg Asp Phe Tyr Glu Ser Met Phe Pro Ile Pro Ser Gln Phe Glu Leu
                245                 250                 255

Pro Arg Glu Tyr Arg Asn Arg Phe Leu His Met His Glu Leu Gln Glu
            260                 265                 270

Trp Arg Ala Tyr Arg Asp Lys Leu Lys Phe Trp Thr His Cys Val Leu
            275                 280                 285

Ala Thr Leu Ile Met Phe Thr Ile Phe Ser Phe Phe Ala Glu Gln Leu
    290                 295                 300
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Ile Ala Leu Lys Arg Lys Ile Phe Pro Arg Arg Arg Ile His Lys Glu
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Ala Ser Pro Asn Arg Ile Arg Val
              325


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<223>

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Met Ala Ala Gly Leu Ala Arg Leu Leu Leu Leu Gly Leu Ser Ala
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Gly Gly Pro Ala Pro Ala Gly Ala Ala Lys Met Lys Val Val Glu Glu
              20              25              30

Pro Asn Ala Phe Gly Val Asn Asn Pro Phe Leu Pro Gln Ala Ser Arg
              35              40              45

Leu Gln Ala Lys Arg Asp Pro Ser Pro Val Ser Gly Pro Val His Leu
   50              55              60

Phe Arg Leu Ser Gly Lys Cys Phe Ser Leu Val Glu Ser Thr Tyr Lys
65              70              75              80

Tyr Glu Phe Cys Pro Phe His Asn Val Thr Gln His Glu Gln Thr Phe
              85              90              95

Arg Trp Asn Ala Tyr Ser Gly Ile Leu Gly Ile Trp His Glu Trp Glu
              100              105              110

Ile Ala Asn Asn Thr Phe Thr Gly Met Trp Met Arg Asp Gly Asp Ala
        115              120              125

Cys Arg Ser Arg Ser Arg Gln Ser Lys Val Glu Leu Ala Cys Gly Lys
   130              135              140

Ser Asn Arg Leu Ala His Val Ser Glu Pro Ser Thr Cys Val Tyr Ala
145              150              155              160

Leu Thr Phe Glu Thr Pro Leu Val Cys His Pro His Ala Leu Leu Val
              165              170              175

Tyr Pro Thr Leu Pro Glu Ala Leu Gln Arg Gln Trp Asp Gln Val Glu
              180              185              190
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Gln Asp Leu Ala Asp Glu Leu Ile Thr Pro Gln Gly His Glu Lys Leu
        195                 200                 205

Leu Arg Thr Leu Phe Glu Asp Ala Gly Tyr Leu Lys Thr Pro Glu Glu
    210                 215                 220

Asn Glu Pro Thr Gln Leu Glu Gly Gly Pro Asp Ser Leu Gly Phe Glu
225                 230                 235                 240

Thr Leu Glu Asn Cys Arg Lys Ala His Lys Glu Leu Ser Lys Glu Ile
                245                 250                 255

Lys Arg Leu Lys Gly Leu Leu Thr Gln His Gly Ile Pro Tyr Thr Arg
                260                 265                 270

Pro Thr Glu Thr Ser Asn Leu Glu His Leu Gly His Glu Thr Pro Arg
            275                 280                 285

Ala Lys Ser Pro Glu Gln Leu Arg Gly Asp Pro Gly Leu Arg Gly Ser
        290                 295                 300

Leu
305
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ggcgctcag gctcctcggg gcgtggcgtg gcggtgaagg ggtgatgctg ttcaagctcc         180

tgcagagaca aacctatacc tgcctgtccc acaggtatgg gctctacgtg tgcttcttgg        240

gcgtcgttgt caccatcgtc tccgccttcc agttcggaga ggtggttctg gaatgggagcc      300

gagatcaata ccatgttttg tttgattcct atagagacaa tattgctgga aagtcctttc       360

agaatcggct ttgtctgccc atgccgattg acgttgttta cacctgggtg aatggcacag      420

atcttgaact actgaaggaa ctacagcagg tcagagaaca gatggaggag gagcagaaag      480

caatgagaga aatccttggg aaaaacacaa cggaacctac taagaagagt gagaagcagt      540

tagagtgttt gctaacacac tgcattaagg tgccaatgct tgtactggac ccagccctgc      600

cagccaacat caccctgaag gacgtgccat ctctttatcc ttctttcat tctgccagtg        660

acattttcaa tgttgcaaaa ccaaaaaacc cttctaccaa tgtctcagtt gttgttttg        720

acagtactaa ggatgttgaa gatgcccact ctggactgct taaaggaaat agcagacaga      780

cagtatggag ggggtacttg acaacagata aagaagtccc tggattagtg ctaatgcaag      840

atttggcttt cctgagtgga tttccaccaa cattcaagga aacaaatcaa ctaaaaacaa      900
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agaacatgac cattgatgga aaagaactga ccataagtcc tgcatattta ttatgggatc     1080

tgagcgccat cagccagtct aagcaggatg aagacatctc tgccagtcgt tttgaagata     1140

acgaagaact gaggtactca ttgcgatcta tcgagaggca tgcaccatgg gttcggaata     1200

ttttcattgt caccaacggg cagattccat cctggctgaa ccttgacaat cctcgagtga     1260

caatagtaac acaccaggat gtttttcgaa atttgagcca cttgcctacc tttagttcac     1320

ctgctattga aagtcacatt catcgcatcg aagggctgtc ccagaagttt atttacctaa     1380

atgatgatgt catgtttggg aaggatgtct ggccagatga ttttttacagt cactccaaag     1440

gccagaaggt ttatttgaca tggcctgtgc caaactgtgc cgagggctgc ccaggttcct     1500

ggattaagga tggctattgt gacaaggctt gtaataattc agcctgcgat tgggatggtg     1560

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ttcgagcatgc ttctattgcc aacaagtgga aaaccatcca cctcataatg cacagtggaa     1980

tgaattgccac cacaatacat tttaatctca cgtttcaaaa tacaaacgat gaagagttca     2040

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agaagggtta cgaaaattta gttagtccca taacacttct tccagaggcg gaaatccttt     2160

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caaggagagc ccaggaagag gtgaaaattc ccctggtaaa tatttcactc cttccaaaag     2280

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agaggttgac ttttcctgca gtgagtgtaa aagtgaatgg tcatgaccag ggtcagaatc     2580

caccctgga cttggagacc acagcaagat ttagagtgga aactcacacc caaaaaacca     2640

taggcggaaa tgtgacaaaa gaaaagcccc catctctgat tgttccactg gaaagccaga     2700

tgacaaaaga aagaaaatc acagggaaag aaaaagagaa cagtagaatg gaggaaaatg     2760
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aagaagagtc attgaagaca caattggcat acttcactga tagcaaaaat actgggaggc   2940

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ttggattcac atcgcggaaa gtccctgctc acatgcctca catgattgac cggattgtta   3060

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acaaagaagc tagtcccaat cgaatcagag tatagaagat cttcatttga aaaccatcta   3960

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gggatccttc acccgtgtct ggacccgtgc atctcttccg actctcgggc aagtgcttca     240

gcctggtgga gtccacgtac aagtatgagt tctgcccgtt ccacaacgtg acccagcacg     300

agcagacctt ccgctggaac gcctacagtg ggatcctcgg catctggcac gagtgggaga     360

tcgccaacaa caccttcacg ggcatgtgga tgagggacgg tgacgcctgc cgttcccgga     420

gccggcagag caaggtggag ctggcgtgtg gaaaaagcaa ccggctggcc catgtgtccg     480

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aggacctggc cgatgagctg atcaccccccc agggccatga gaagttgctg aggacacttt     660

ttgaggatgc tggctactta aagaccccag aagaaatga acccacccag ctggagggag     720
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ccacagaaac ttccaacttg gagcacttgg gccacgagac gcccagagcc aagtctccag    900

agcagctgcg gggtgaccca ggactgcgtg ggagtttgtg accttgtggt gggagagcag    960

aggtggacgc ggccgagagc cctacagaga agctggctgg taggacccgc aggaccagct    1020

gaccaggctt gtgctcagag aagcagacaa aacaaagatt caaggtttta attaattccc    1080

atactgataa aaataactcc atgaattctg taaaccattg cataaatgct atagtgtaaa    1140

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            20                  25                  30

Asp Asp Asp Leu Leu Leu Pro Tyr Pro Arg Ala Arg Ala Arg Leu Pro
        35                  40                  45

Arg Asp Cys Thr Arg Val Arg Ala Gly Asn Arg Glu His Glu Ser Trp
    50                  55                  60

Pro Pro Pro Pro Ala Thr Pro Gly Ala Gly Gly Leu Ala Val Arg Thr
65                  70                  75                  80

Phe Val Ser His Phe Arg Asp Arg Ala Val Ala Gly His Leu Thr Arg
                85                  90                  95

Ala Val Glu Pro Leu Arg Thr Phe Ser Val Leu Glu Pro Gly Gly Pro
                100                 105                 110

Gly Gly Cys Ala Ala Arg Arg Arg Ala Thr Val Glu Glu Thr Ala Arg
            115                 120                 125

Ala Ala Asp Cys Arg Val Ala Gln Asn Gly Gly Phe Phe Arg Met Asn
    130                 135                 140
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Ser Gly Glu Cys Leu Gly Asn Val Val Ser Asp Glu Arg Arg Val Ser
145                 150                 155                 160

Ser Ser Gly Gly Leu Gln Asn Ala Gln Phe Gly Ile Arg Arg Asp Gly
                165                 170                 175

Thr Leu Val Thr Gly Tyr Leu Ser Glu Glu Glu Val Leu Asp Thr Glu
                180                 185                 190

Asn Pro Phe Val Gln Leu Leu Ser Gly Val Val Trp Leu Ile Arg Asn
            195                 200                 205

Gly Ser Ile Tyr Ile Asn Glu Ser Gln Ala Thr Glu Cys Asp Glu Thr
    210                 215                 220

Gln Glu Thr Gly Ser Phe Ser Lys Phe Val Asn Val Ile Ser Ala Arg
225                 230                 235                 240

Thr Ala Ile Gly His Asp Arg Lys Gly Gln Leu Val Leu Phe His Ala
245                 250                 255

Asp Gly His Thr Glu Gln Arg Gly Ile Asn Leu Trp Glu Met Ala Glu
            260                 265                 270

Phe Leu Leu Lys Gln Asp Val Val Asn Ala Ile Asn Leu Asp Gly Gly
        275                 280                 285

Gly Ser Ala Thr Phe Val Leu Asn Gly Thr Leu Ala Ser Tyr Pro Ser
    290                 295                 300

Asp His Cys Gln Asp Asn Met Trp Arg Cys Pro Arg Gln Val Ser Thr
305                 310                 315                 320

Val Val Cys Val His Glu Pro Arg Cys Gln Pro Pro Asp Cys His Gly
                325                 330                 335

His Gly Thr Cys Val Asp Gly His Cys Gln Cys Thr Gly His Phe Trp
            340                 345                 350

Arg Gly Pro Gly Cys Asp Glu Leu Asp Cys Gly Pro Ser Asn Cys Ser
        355                 360                 365

Gln His Gly Leu Cys Thr Glu Thr Gly Cys Arg Cys Asp Ala Gly Trp
    370                 375                 380

Thr Gly Ser Asn Cys Ser Glu Glu Cys Pro Leu Gly Trp His Gly Pro
385                 390                 395                 400
```

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Gly Cys Gln Arg Arg Cys Lys Cys Glu His His Cys Pro Cys Asp Pro
            405             410             415

Lys Thr Gly Asn Cys Ser Val Ser Arg Val Lys Gln Cys Leu Gln Pro
            420             425             430

Pro Glu Ala Thr Leu Arg Ala Gly Glu Leu Ser Phe Phe Thr Arg Thr
        435             440             445

Ala Trp Leu Ala Leu Thr Leu Ala Leu Ala Phe Leu Leu Leu Ile Ser
    450             455             460

Ile Ala Ala Asn Leu Ser Leu Leu Leu Ser Arg Ala Glu Arg Asn Arg
465             470             475             480

Arg Leu His Gly Asp Tyr Ala Tyr His Pro Leu Gln Glu Met Asn Gly
            485             490             495

Glu Pro Leu Ala Ala Glu Lys Glu Gln Pro Gly Gly Ala His Asn Pro
        500             505             510

Phe Lys Asp
    515
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ccacgcgcgc gcgcgcgcct cccccgggac tgcacacggg tgcgcgccgg caaccgcgag     180

cacgagagtt ggcctccgcc tcccgcgact cccggcgccg gcggtctggc cgtgcgcacc     240

ttcgtgtcgc acttcaggga ccgcgcggtg gccggccacc tgacgcgggc cgttgagccc     300

ctgcgcacct tctcggtgct ggagcccggt ggacccggcg gctgcgcggc gagacgacgc     360

gccaccgtgg aggagacggc gcgggcggcc gactgccgtg tcgcccagaa cggcggcttc     420

ttccgcatga actcgggcga gtgcctgggg aacgtggtga gcgacgagcg gcgggtgagc     480

agctccgggg ggctgcagaa cgcgcagttc gggatccgcc gcgacgggac cctggtcacc     540

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gggtcgtgt ggctgattcg taatggaagc atctacatca acgagagcca agccacagag     660

tgtgacgaga cacaggagac aggttccttt agcaaatttg tgaatgtgat atcagccagg     720

acggccattg gccacgaccg gaaagggcag ctggtgctct ttcatgcaga cggccatacg     780

gagcagcgtg gcatcaacct gtgggaaatg gcggagttcc tgctgaaaca ggacgtggtc     840
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aacgccatca  acctggatgg  gggtggctct  gccacctttg  tgctcaacgg  gaccttggcc      900

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gtggtgtgtg  tgcacgaacc  ccgctgccag  ccgcctgact  gccacgggcca  cgggacctgc     1020

gtggacgggc  actgccaatg  caccgggcac  ttctggcggg  gtcccggctg  tgatgagctg     1080

gactgtggcc  cctctaactg  cagccagcac  ggactgtgca  cggagaccgg  ctgccgctgt     1140

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Asp Thr Phe Ala Asp Ser Leu Arg Tyr Val Asn Lys Ile Leu Asn Ser
1               5                   10                  15

Lys Phe Gly Phe Thr Ser Arg Lys Val Pro Ala His Met Pro His Met
            20                  25                  30

Ile Asp Arg Ile Val Met Gln Glu Leu Gln Asp Met Phe Pro Glu Glu
        35                  40                  45

Phe Asp Lys Thr Ser Phe His Lys Val Arg His Ser Glu Asp Met Gln
```

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         50                      55                      60

Phe Ala Phe Ser Tyr Phe Tyr Tyr Leu Met Ser Ala Val Gln Pro Leu
65                      70                      75                      80

Asn Ile Ser Gln Val Phe His Glu Val Asp Thr Asp Gln Ser Gly Val
                        85                      90                      95

Leu Ser Asp Arg Glu Ile Arg Thr Leu Ala Thr Arg Ile His Asp Leu
                100                     105                     110

Pro Leu Ser Leu Gln Asp Leu Thr Gly Leu Glu His Met Leu Ile Asn
        115                     120                     125

Cys Ser Lys Met Leu Pro Ala Asn Ile Thr Gln Leu Asn Asn Ile Pro
        130                     135                     140

Pro Thr Gln Glu Ala Tyr Tyr Asp Pro Asn Leu Pro Pro Val Thr Lys
145                     150                     155                     160

Ser Leu Val Thr Asn Cys Lys Pro Val Thr Asp Lys Ile His Lys Ala
                165                     170                     175

Tyr Lys Asp Lys Asn Lys Tyr Arg Phe Glu Ile Met Gly Glu Glu Glu
        180                     185                     190

Ile Ala Phe Lys Met Ile Arg Thr Asn Val Ser His Val Val Gly Gln
        195                     200                     205

Leu Asp Asp Ile Arg Lys Asn Pro Arg Lys Phe Val Cys Leu Asn Asp
210                     215                     220

Asn Ile Asp His Asn His Lys Asp Ala Arg Thr Val Lys Ala Val Leu
225                     230                     235                     240

Arg Asp Phe Tyr Glu Ser Met Phe Pro Ile Pro Ser Gln Phe Glu Leu
                245                     250                     255

Pro Arg Glu Tyr Arg Asn Arg Phe Leu His Met His Glu Leu Gln Glu
        260                     265                     270

Trp Arg Ala Tyr Arg Asp Lys Leu Lys Phe Trp Thr His Cys Val Leu
        275                     280                     285

Ala Thr Leu Ile Ile Phe Thr Ile Phe Ser Phe Phe Ala Glu Gln Ile
        290                     295                     300
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                                    -15-

Ile Ala Leu Lys Arg Lys Ile Phe Pro Arg Arg Arg Ile His Lys Glu
305   310   315   320

Ala Ser Pro Asp Arg Ile Arg Val
                325

<210> 9 <211> 307 <212> PRT <213> Mus musculus <400> 9

Met Ala Gly Arg Leu Ala Gly Phe Leu Met Leu Leu Gly Leu Ala Ser
1   5   10   15

Gln Gly Pro Ala Pro Ala Cys Ala Gly Lys Met Lys Val Val Glu Glu
            20   25   30

Pro Asn Thr Phe Gly Leu Asn Asn Pro Phe Leu Pro Gln Ala Ser Arg
            35   40   45

Leu Gln Pro Lys Arg Glu Pro Ser Ala Val Ser Gly Pro Leu His Leu
    50   55   60

Phe Arg Leu Ala Gly Lys Cys Phe Ser Leu Val Glu Ser Thr Tyr Lys
65   70   75   80

Tyr Glu Phe Cys Pro Phe His Asn Val Thr Gln His Glu Gln Thr Phe
                85   90   95

Arg Trp Asn Ala Tyr Ser Gly Ile Leu Gly Ile Trp His Glu Trp Glu
            100   105   110

Ile Ile Asn Asn Thr Phe Lys Gly Met Trp Met Thr Asp Gly Asp Ser
    115   120   125

Cys His Ser Arg Ser Arg Gln Ser Lys Val Glu Leu Thr Cys Gly Lys
    130   135   140

Ile Asn Arg Leu Ala His Val Ser Glu Pro Ser Thr Cys Val Tyr Ala
145   150   155   160

Leu Thr Phe Glu Thr Pro Leu Val Cys His Pro His Ser Leu Leu Val
                165   170   175

Tyr Pro Thr Leu Ser Glu Ala Leu Gln Gln Arg Leu Asp Gln Val Glu
                180   185   190

Gln Asp Leu Ala Asp Glu Leu Ile Thr Pro Gln Gly Tyr Glu Lys Leu
    195   200   205

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Leu Arg Val Leu Phe Glu Asp Ala Gly Tyr Leu Lys Val Pro Gly Glu
    210                 215                 220

Thr His Pro Thr Gln Leu Ala Gly Gly Ser Lys Gly Leu Gly Leu Glu
225                 230                 235                 240

Thr Leu Asp Asn Cys Arg Lys Ala His Ala Glu Leu Ser Gln Glu Val
                245                 250                 255

Gln Arg Leu Thr Ser Leu Leu Gln Gln His Gly Ile Pro His Thr Gln
            260                 265                 270

Pro Thr Glu Thr Thr His Ser Gln His Leu Gly Gln Gln Leu Pro Ile
        275                 280                 285

Gly Ala Ile Ala Ala Glu His Leu Arg Ser Asp Pro Gly Leu Arg Gly
    290                 295                 300

Asn Ile Leu
305
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<210> 10 <211> 2070 <212> DNA <213> Mus musculus <220> <221> misc_feature <222>
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cattcaggtg agcggatcac ggtcctgcgg cttgggggacc gagcctggct ggttcttctg     180

acctttcaa ttccataggc tgaataaccc gttcttgccc caggcaagcc gccttcagcc     240

caagagagag ccttcagctg tatcccgcaa attaagagaa attaatttca aacgatttag     300

aaagtattct agccaggcga tgatggcgca cgcctttaat cccagcactt gggaggcaga     360

ggcaggcaga tttccgagtt caaggccatc agaactgact gtacatctta gtacagttta     420

gcatgtgatc agagatctga atcacaaagc tgggcctgcg tggtaaagca ggtcctttct     480

aataaggttg cagtttagat tttctttctt aactcttttta ttctttgaga cagggtttct     540

caacagtggg tgtcctggaa ctcacttttg taaaccaggc tgcccttaaa ctcacaaagc     600

tctgtcagcc tctgcctcct gagtgctggg attaaaggtc cacaccctgt tcattcattt     660

ttaatttttg agactgggtc tcattatgtg gcccctagaca gatactgaga gcctcctcca     720

caggaacaag catgggaatc ctgccacaga caaccagttc tgtggtctgg agatgagttt     780

gtcagtccct aggagttagg tcagcctgcc tctgcattcc caataattta ggaaaggagc     840

ttggggcgtt ctggccttga tggttagtgc cctcctgcca accttagctt ccagctttag     900
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tatgaattct gcccctttcca caacgtcacc cagcacgagc agaccttccg ctggaatgcc     1140

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agcagagcat ctgcggagtg acccaggact acgtgggaac atcctgtgag caaggtggcc     1860

acgaagaata gaaatatcct gagctttgag tgtcctttca cagagtgaac aaaactggtg     1920

tggtgtagac acggcttctt ttggcatatt ctagatcaga cagtgtcact gacaaacaag     1980

agggacctgc tggccagcct ttgttgtgcc caaagatcca gacaaaataa agattcaaag     2040

ttttaattaa aaaaaaaaaa aaggaattc                                       2070

<210>   11 <211>  113 <212>   PRT <213>   Rattus rattus   <400>   11

Phe Pro Pro Thr Phe Lys Glu Thr Ser Gln Leu Lys Thr Lys Leu Pro
1               5                   10                  15

Glu Asn Leu Ser Ser Lys Ile Lys Leu Leu Gln Leu Tyr Ser Glu Ala
                20                  25                  30

Ser Val Ala Leu Leu Lys Leu Asn Asn Pro Lys Gly Phe Pro Glu Leu
            35                  40                  45

Asn Lys Gln Thr Lys Lys Asn Met Ser Ile Ser Gly Lys Glu Leu Ala
        50                  55                  60

Ile Ser Pro Ala Tyr Leu Leu Trp Asp Leu Ser Ala Ile Ser Gln Ser
65                  70                  75                  80
```

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Lys Gln Asp Glu Asp Val Ser Ala Ser Arg Phe Glu Asp Asn Glu Glu
                85   90   95

Leu Arg Tyr Ser Leu Arg Ser Ile Glu Arg His Asp Ser Met Ser Pro
            100   105   110

Leu

<210> 12 <211> 460 <212> DNA <213> Rattus rattus <400> 12
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taaccccaaa ggtttccccg agctgaacaa gcagaccaag aagaacatga gcatcagtgg   180

gaaggaactg gccatcagcc ctgcctatct gctgtgggac ctgagcgcca tcagccagtc   240

caagcaggat gaagatgtgt ctgccagccg cttcgaggat aacgaagagc tgaggtactc   300

actggatct atcgagagac atgattccat gagtcctttta tgaattctgg ccatatcttc   360

aatgatgatc tcagtagtat tcctctgaaa tggcacacat ttttctaatg agaacttgaa   420

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<210> 13 <211> 502 <212> PRT <213> Drosophila melanogaster <400> 13

Gly Thr Arg Arg Phe Asp Asp Lys Asn Glu Leu Arg Tyr Ser Leu Arg
1   5   10   15

Ser Leu Glu Lys His Ala Ala Trp Ile Arg His Val Tyr Ile Val Thr
            20   25   30

Asn Gly Gln Ile Pro Ser Trp Leu Asp Leu Ser Tyr Glu Arg Val Thr
        35   40   45

Val Val Pro His Glu Val Leu Ala Pro Asp Pro Asp Gln Leu Pro Thr
    50   55   60

Phe Ser Ser Ser Ala Ile Glu Thr Phe Leu His Arg Ile Pro Lys Leu
65   70   75   80

Ser Lys Arg Phe Leu Tyr Leu Asn Asp Asp Ile Phe Leu Gly Ala Pro
                85   90   95

Leu Tyr Pro Glu Asp Leu Tyr Thr Glu Ala Glu Gly Val Arg Val Tyr
            100   105   110

Gln Ala Trp Met Val Pro Gly Cys Ala Leu Asp Cys Pro Trp Thr Tyr
        115   120   125

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```
Ile Gly Asp Gly Ala Cys Asp Arg His Cys Asn Ile Asp Ala Cys Gln
    130                 135                 140

Phe Asp Gly Gly Asp Cys Ser Glu Thr Gly Pro Ala Ser Asp Ala His
145                 150                 155                 160

Val Ile Pro Pro Ser Lys Glu Val Leu Glu Val Gln Pro Ala Ala Val
                165                 170                 175

Pro Gln Ser Arg Val His Arg Phe Pro Gln Met Gly Leu Gln Lys Leu
                180                 185                 190

Phe Arg Arg Ser Ser Ala Asn Phe Lys Asp Val Met Arg His Arg Asn
                195                 200                 205

Val Ser Thr Leu Lys Glu Leu Arg Arg Ile Val Glu Arg Phe Asn Lys
    210                 215                 220

Ala Lys Leu Met Ser Leu Asn Pro Glu Leu Glu Thr Ser Ser Ser Glu
225                 230                 235                 240

Pro Gln Thr Thr Gln Arg His Gly Leu Arg Lys Glu Asp Phe Lys Ser
                245                 250                 255

Ser Thr Asp Ile Tyr Ser His Ser Leu Ile Ala Thr Asn Met Leu Leu
                260                 265                 270

Asn Arg Ala Tyr Gly Phe Lys Ala Arg His Val Leu Ala His Val Gly
    275                 280                 285

Phe Leu Ile Asp Lys Asp Ile Val Glu Ala Met Gln Arg Arg Phe His
    290                 295                 300

Gln Gln Ile Leu Asp Thr Ala His Gln Arg Phe Arg Ala Pro Thr Asp
305                 310                 315                 320

Leu Gln Tyr Ala Phe Ala Tyr Tyr Ser Phe Leu Met Ser Glu Thr Lys
                325                 330                 335

Val Met Ser Val Glu Glu Ile Phe Asp Glu Phe Asp Thr Asp Gly Ser
                340                 345                 350

Ala Thr Trp Ser Asp Arg Glu Val Arg Thr Phe Leu Thr Arg Ile Tyr
    355                 360                 365

Gln Pro Pro Leu Asp Trp Ser Ala Met Arg Tyr Phe Glu Glu Val Val
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```
Gln Asn Cys Thr Arg Asn Leu Gly Met His Leu Lys Val Asp Thr Val
385                 390                 395                 400

Glu His Ser Thr Leu Val Tyr Glu Arg Tyr Glu Asp Ser Asn Leu Pro
                405                 410                 415

Thr Ile Thr Arg Asp Leu Val Val Arg Cys Pro Leu Leu Ala Glu Ala
            420                 425                 430

Leu Ala Ala Asn Phe Ala Val Arg Pro Lys Tyr Asn Phe His Val Ser
        435                 440                 445

Pro Lys Arg Thr Ser His Ser Asn Phe Met Met Leu Thr Ser Asn Leu
    450                 455                 460

Thr Glu Val Val Glu Ser Leu Asp Arg Leu Arg Arg Asn Pro Arg Lys
465                 470                 475                 480

Phe Asn Cys Ile Asn Asp Asn Leu Asp Ala Asn Arg Gly Glu Asp Asn
                485                 490                 495

Glu Asp Gly Ala Pro Ser
            500
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<210> 14 <211> 9792 <212>   DNA <213> Mus musculus <400> 14

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cagactttct acagccaatt ctcttcttcc tcctctccat gggttcaggg tcttcatctc    180
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cagaaggaac tagggcttta agcacgagaa gcaagttctg tacagactta cacaggccca    960

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cacccacgaa ccccgggcgc caagccacca cgcggccgtg cgcaccttcg tgtcgcactt    1500

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cagccagtgt caccactgtt gatcttaggt tttcacagat cctaaaactt ctgccagtga    2460

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cccctattgc tcctttacaa tggtccactg acctgctcac ctctactttt ttttttttaa    2640
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Tyr His Val Leu Phe Asp Ser Tyr Arg Asp Asn Ile Ala Gly Lys Ser
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Phe Gln Asn Arg Leu Cys Leu Pro Met Pro Ile Asp Val Val Tyr Thr
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Trp Val Asn Gly Thr Asp Leu Glu Leu Leu Lys Glu Leu Gln Gln Val
                  85                   90                   95

Arg Glu His Met Glu Glu Glu Gln Arg Ala Met Arg Glu Thr Leu Gly
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Lys Asn Thr Thr Glu Pro Thr Lys Lys Ser Glu Lys Gln Leu Glu Cys
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Leu Leu Thr His Cys Ile Lys Val Pro Met Leu Val Leu Asp Pro Ala
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Leu Pro Ala Thr Ile Thr Leu Lys Asp Leu Pro Thr Leu Tyr Pro Ser
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Phe His Ala Ser Ser Asp Met Phe Asn Val Ala Lys Pro Lys Asn Pro
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Ser Thr Asn Val Pro Val Val Val Phe Asp Thr Thr Lys Asp Val Glu
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Asp Ala His Ala Gly Pro Phe Lys Gly Gly Gln Gln Thr Asp Val Trp
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Arg Ala Tyr Leu Thr Thr Asp Lys Asp Ala Pro Gly Leu Val Leu Ile
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Gln Gly Leu Ala Phe Leu Ser Gly Phe Pro Pro Thr Phe Lys Glu Thr
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Ser Gln Leu Lys Thr Lys Leu Pro Arg Lys Ala Phe Pro Leu Lys Ile
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Lys Leu Leu Arg Leu Tyr Ser Glu Ala Ser Val Ala Leu Leu Lys Leu
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Ala Ser Arg Phe Glu Asp Asn Glu Glu Leu Arg Tyr Ser Leu Arg Ser
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Ile Glu Arg His Ala Pro Trp Val Arg Asn Ile Phe Ile Val Thr Asn
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Gly Gln Ile Pro Ser Trp Leu Asn Leu Asp Asn Pro Arg Val Thr Ile
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Val Thr His Gln Asp Ile Phe Gln Asn Leu Ser His Leu Pro Thr Phe
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Ser Ser Pro Ala Ile Glu Ser His Ile His Arg Ile Glu Gly Leu Ser
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Gln Lys Phe Ile Tyr Leu Asn Asp Asp Val Met Phe Gly Lys Asp Val
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Trp Pro Asp Asp Phe Tyr Ser His Ser Lys Gly Gln Lys Val Tyr Leu
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Thr Trp Pro Val Pro Asn Cys Ala Glu Gly Cys Pro Gly Ser Trp Ile
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Lys Asp Gly Tyr Cys Asp Lys Ala Cys Asn Thr Ser Pro Cys Asp Trp
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Asp Gly Gly Asn Cys Ser Gly Asn Thr Ala Gly Asn Arg Phe Val Ala
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Arg Gly Gly Gly Thr Gly Asn Ile Gly Ala Gly Gln His Trp Gln Phe
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Gly Gly Gly Ile Asn Thr Ile Ser Tyr Cys Asn Gln Gly Cys Ala Asn
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Ile Glu Gly Thr Tyr Ser Asp Asn Pro Ile Ile Arg His Ala Ser Ile
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Ala Asn Lys Trp Lys Thr Leu His Leu Ile Met Pro Gly Gly Met Asn
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Ala Thr Thr Ile Tyr Phe Asn Leu Thr Leu Gln Asn Ala Asn Asp Glu
    610             615             620

Glu Phe Lys Ile Gln Ile Ala Val Glu Val Asp Thr Arg Glu Ala Pro
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Lys Leu Asn Ser Thr Thr Gln Lys Ala Tyr Glu Ser Leu Val Ser Pro
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Val Thr Pro Leu Pro Gln Ala Asp Val Pro Phe Glu Asp Val Pro Lys
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Glu Lys Arg Phe Pro Lys Ile Arg Arg His Asp Val Asn Ala Thr Gly
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Arg Phe Gln Glu Glu Val Lys Ile Pro Arg Val Asn Ile Ser Leu Leu
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Pro Lys Glu Ala Gln Val Arg Leu Ser Asn Leu Asp Leu Gln Leu Glu
705             710             715                         720

Arg Gly Asp Ile Thr Leu Lys Gly Tyr Asn Leu Ser Lys Ser Ala Leu
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Leu Arg Ser Phe Leu Gly Asn Ser Leu Asp Thr Lys Ile Lys Pro Gln
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Ala Arg Thr Asp Glu Thr Lys Gly Asn Leu Glu Val Pro Gln Glu Asn
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Pro Ser His Arg Arg Pro His Gly Phe Ala Gly Glu His Arg Ser Glu
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Ala Leu Asn Pro Pro Val Leu Glu Thr Asn Ala Arg Leu Ala Gln
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Pro Thr Leu Gly Val Thr Val Ser Lys Glu Asn Leu Ser Pro Leu Ile
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Val Pro Pro Glu Ser His Leu Pro Lys Glu Glu Glu Ser Asp Arg Ala
               835   840   845

Glu Gly Asn Ala Val Pro Val Lys Glu Leu Val Pro Gly Arg Arg Leu
           850   855   860

Gln Gln Asn Tyr Pro Gly Phe Leu Pro Trp Glu Lys Lys Lys Tyr Phe
865   870   875   880

Gln Asp Leu Leu Asp Glu Glu Glu Ser Leu Lys Thr Gln Leu Ala Tyr
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Phe Thr Asp Arg Lys His Thr Gly Arg Gln Leu Lys
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gccccaacag atttgcagta cgcattcgct tactacttct ttctaatgag cgaaatccaa    1020

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Ser His Ala Ala Val Arg Thr Phe Val Ser His Phe Glu Gly Arg
    50                  55                  60

Ala Val Ala Gly His Leu Thr Arg Val Ala Asp Pro Leu Arg Thr Phe
65                  70                  75                  80

Ser Val Leu Glu Pro Gly Gly Ala Gly Gly Cys Gly Gly Arg Ser Ala
                85                  90                  95

Ala Ala Thr Val Glu Asp Thr Ala Val Arg Ala Gly Cys Arg Ile Ala
            100                 105                 110

Gln Asn Gly Gly Phe Phe Arg Met Ser Thr Gly Glu Cys Leu Gly Asn
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Val Val Ser Asp Gly Arg Leu Val Ser Ser Ser Gly Gly Leu Gln Asn
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-35-

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Leu Glu Glu Glu Val Leu Asp Pro Val Asn Pro Phe Val Gln Leu Leu
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Ser Gly Val Val Trp Leu Ile Arg Asn Gly Asn Ile Tyr Ile Asn Glu
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Ser Gln Ala Ile Glu Cys Asp Glu Thr Gln Glu Thr Gly Ser Phe Ser
            195             200             205

Lys Phe Val Asn Val Met Ser Ala Arg Thr Ala Val Gly His Asp Arg
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Glu Gly Gln Leu Ile Leu Phe His Ala Asp Gly Gln Thr Glu Gln Arg
225             230             235                     240

Gly Leu Asn Leu Trp Glu Met Ala Glu Phe Leu Arg Gln Gln Asp Val
                245             250                     255

Val Asn Ala Ile Asn Leu Asp Gly Gly Gly Ser Ala Thr Phe Val Leu
            260             265             270

Asn Gly Thr Leu Ala Ser Tyr Pro Ser Asp His Cys Gln Asp Asn Met
        275             280             285

Trp Arg Cys Pro Arg Gln Val Ser Thr Val Val Cys Val His Glu Pro
        290             295             300

Arg Cys Gln Pro Pro Asp Cys Ser Gly His Gly Thr Cys Val Asp Gly
305             310             315                     320

His Cys Glu Cys Thr Ser His Phe Trp Arg Gly Glu Ala Cys Ser Glu
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Leu Asp Cys Gly Pro Ser Asn Cys Ser Gln His Gly Leu Cys Thr Ala
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Gly Cys His Cys Asp Ala Gly Trp Thr Gly Ser Asn Cys Ser Glu Glu
        355             360             365

Cys Pro Leu Gly Trp Tyr Gly Pro Gly Cys Gln Arg Pro Cys Gln Cys
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Glu His Gln Cys Phe Cys Asp Pro Gln Thr Gly Asn Cys Ser Ile Ser
385             390             395                     400
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Leu Ile Phe Leu Leu Leu Ile Ser Thr Gly Val Asn Val Ser Leu Phe
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Leu Gly Ser Arg Ala Glu Arg Asn Arg His Leu Asp Gly Asp Tyr Val
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Tyr His Pro Leu Gln Glu Val Asn Gly Glu Ala Leu Thr Ala Glu Lys
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Pro Ala Ala Gln Thr Ala Gly Ala His Arg Pro Ser Val Arg Thr Phe
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Asp Thr Glu Asn
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1   5   10   15

Lys Phe Gly Phe Thr Ser Arg Lys Val Pro Ala His
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1   5   10   15

Pro Phe Leu Pro Gln
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Ile Leu Asn Ser Lys
1   5

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1   5   10   15

Lys

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Asn Val Ala Lys Pro Lys
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